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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,043	03/30/2006	Nobuo Sakaguchi	4456-0104PUS1	2803

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EXAMINER
HAMA, JOANNE

ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
11/16/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/534,043	SAKAGUCHI, NOBUO	
	Examiner	Art Unit	
	JOANNE HAMA	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,6 and 12-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,6 and 12-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 29, 2009 has been entered.

Applicant has filed a supplemental response on July 23, 2009.

With regard claim amendments filed December 29, 2008, claims 1, 3, 5, 12, 15, 17-19 are amended. Claims 4, 7-11 are cancelled.

With regard to the claim amendments filed June 29, 2009, claims 1, 5 are amended. Claims 3, 4, 7-11 are cancelled.

Claims 1, 2, 5, 6, 12-19, drawn to a transgenic non-human mammal comprising a GANP gene, are under consideration.

Withdrawn Objection/Rejection

Claim Objection

Applicant's arguments, see claim amendments filed December 29, 2009, with respect to the objection of claim 15 have been fully considered and are persuasive. Applicant has amended the claim. The objection of claim 15 has been withdrawn.

35 USC § 112, 2nd parag.

Applicant's arguments, see claim amendments filed December 29, 2009, with respect to the rejection of claims 17-19 have been fully considered and are persuasive. Applicant has amended the claims. The rejection of claims 17-19 has been withdrawn.

35 USC §103(a)

Applicant's arguments, see claim amendments filed June 29, 2009, with respect to the rejection of claims 1-5 as being unpatentable over Kuwahara et al., 2000, Blood, 95: 2321-2328, previously cited, in view of Jaenisch, 1988, Science, 240: 1468-1474, previously cited, Maas et al., 1999, The Journal of Immunology, 162: 6526-6533, have been fully considered and are persuasive. Applicant has amended the claims to indicate that the non-human mammal produces high affinity antibody-producing B cells. The rejection of claims 17-19 has been withdrawn.

Applicant's arguments, see claim amendments filed June 29, 2009, with respect to the rejection of claims 1, 17-19 as being unpatentable over Kuwahara et al., 2000, Blood, 95: 2321-2328, previously cited, in view of Jaenisch, 1988, Science, 240: 1468-1474, previously cited, Maas et al., 1999, The Journal of Immunology, 162: 6526-6533, previously cited, Henderson et al., 1998, Annu. Rev. Immunol. 16: 163-200, have been fully considered and are persuasive. Applicant has amended the claims to indicate that the non-human mammal produces high affinity antibody-producing B cells. The rejection of claims 17-19 has been withdrawn.

Maintained Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 5, 6, 12-19 remain rejected in modified form under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

a transgenic mouse, or a progeny thereof, comprising a transferred recombinant mouse GANP gene that encodes and expresses a protein of SEQ ID NO. 2, wherein said transgenic mouse produces high affinity antibody-producing B cells,

does not reasonably provide enablement for

any transgenic non-human mammal other than mouse comprising a mouse or human GANP gene, wherein said mammal produces high affinity antibody-producing B cells.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims, for reasons of record October 11, 2007, July 28, 2008, January 21, 2009.

Applicant's arguments filed June 29, 2009 have been fully considered and they are persuasive in part.

With regard to the claims being drawn to ES cells from any species of mammals (Applicant's response, page 6), Applicant has cancelled claim 3. The rejection as it applies to this issue is withdrawn.

With regard to the issue of somatic hypermutation (SHM), wherein Li et al., 2004, teach that while SHM is the predominant mechanism in humans and mice, gene conversion occurs in chickens in other species (Li et al., page 1, 1st col.), Applicant indicates that the claims are limited to bovine, horse, pig, goat, rabbit, dog, cat, mouse, rat, hamster, and guinea pig and that an artisan would recognize that the primary mechanism for generating structurally heterogeneous V regions in mammals is via somatic mutation (Applicant's response, page 7). In response, this is not persuasive. According to the Weill et al., 1996, Review: Immunology Today, 17: 92-97 animal species such as chickens and rabbits exhibit gene conversion, while sheep exhibit hypermutation (Weill et al., page 92, 1st col., 2nd parag.). Given this teaching, it is unclear which mammals recited in claim 1, other than mouse, are able to undergo SHM such that the claimed mammal exhibits high-affinity antibody production in B cells. As such, the claims with respect to this issue are limited to mouse and sheep.

With regard to the Examiner indicating that the application teaches that different lines of mice have different mutations in the HV186.2 region and that an artisan cannot predict which of the mutations is correlated to high affinity binding, Applicant indicates that during the progression of the immune response, hypersomatic mutations generate a population of antibodies with structurally heterogenous V regions. B cells with the highest affinities will be selected to survive. Applicant indicates that GANP increases the rate of somatic hypermutations and result in a greater probability that a rarer high-affinity binding associated mutation will be produced and selected. An artisan does not know a priori which mutations in, e.g., the VH186.2 region will be selected, but the rate

of somatic hypermutation increases in GANP animals (Applicant's response, page 7). In response, this is found persuasive and the rejection as it applies to this issue is withdrawn.

Applicant indicates that according to the Office Action, October 11, pages 7-8, an artisan would not have recognized that the GANP gene could be overexpressed in non-human mammals, other than mice, to obtain the phenotype described in the instant claims. Applicant indicates that undue experimentation is not required to express the transgene in a non-human mammal to obtain a predictable phenotype. Applicant submits Maass et al., 2000, who describes animal models of hypertrophic cardiomyopathy. Exhibit A exemplifies that transgenic animals, other than mice, may be used to obtain predictable phenotype. These animals include mouse, rat, hamster, rabbit, and cat (Applicant's response, page 8). In response, this is not persuasive. While Applicant refers to Maass et al. for teaching that there are a number of transgenic animals of hypertrophic cardiomyopathy, the art teaches that while there are a great number of transgenic animal models, there are also a great number of transgenic animals that produce unexpected phenotypes. As such, while the specification teaches mice comprising a transgene of mouse GANP, the specification provides no guidance for the use of a human GANP transgene or transgenic non-human mammals that express any GANP transgene. Given that predicting phenotypes in transgenic animals is not routine in the art, the rejection as it applies to this issue remains.

With regard to the Examiner indicating that the instant Application is insufficient to demonstrate that GANP transgenic mouse-derived hybridoma clones generate high-

affinity antibodies, Applicant's response of July 23, 2009, page 3, indicates that Figure 28 of the specification teach that transgenic mice generate antibodies with much higher affinity against NP-CG in comparison to wild type mice. As such, an artisan would recognize that the claimed non-human mammals produce high affinity antibodies. In response, this is persuasive, and the regarding this issue is withdrawn.

As such, the claims remain rejected.

It is noted that the rejection of claim 3 is withdrawn as the claim is cancelled.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Mondays, Tuesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance.

Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Joanne Hama/
Primary Examiner
Art Unit 1632